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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/927,788 | 08/09/2001 | Michael J. Mahan | 220002060724 | 6768 |

25226 7590 03/25/2004

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| EXAMINER | |
|---|---|
| PORTNER, VIRGINIA ALLEN | |
| **ART UNIT** | **PAPER NUMBER** |
| 1645 | |

DATE MAILED: 03/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/927,788 | MAHAN ET AL. | |
| | Examiner | Art Unit | |
| | Ginny Portner | 1645 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on *01 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☐ Claim(s) *1-4,7-9,12,13,20,30 and 31* is/are pending in the application.

4a) Of the above claim(s) *30 and 31* is/are withdrawn from consideration.

5)☐ Claim(s) *13 and 20* is/are allowed.

6)☐ Claim(s) *1-4,7-9 and 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) *1-4,7-9, 12,13,20, 30-31* are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

Claims 1,3,and 13 have been amended.

Claims 15,18 and 22 have been canceled.

Claims 30-31 stand with drawn from consideration.

Claims 1-4, 7-9, 12-13 and 20 are under consideration.

### *Allowable Subject Matter*

**1.** Claims 13 and 20 define over the prior art of record and are allowed.

**Rejections Withdrawn**

2. Claims 1 and 7 rejected under 35 U.S.C. 102(b) as being anticipated by Berg et al, has been obviated in light of Applicant's traversal.

**Rejections Maintained**

3. Claims 3-4 rejected under 35 U.S.C. 102(e) as being anticipated by Curtiss, III et al (US Pat. 6,383,496) for reasons of record in paper number 20, dated August 21, 2003.

4. Claims 1-4,7-9 and 12 rejected under 35 U.S.C. 102(b) as being anticipated by Collier et al (US Pat. 5,451,519) for reasons of record in paper number 20, dated August 21, 2003.

5. Claims 1 and 7 rejected under 35 U.S.C. 102(a) as being anticipated by WO98/12206 Shapiro et al, is maintained for reasons of record in paper number 20, dated August 21, 2003.

**Response to Arguments**

6. Applicant's arguments filed December 29, 2003 have been fully considered but they are not persuasive.

7. The rejection of claims 3-4 under 35 U.S.C. 102(e) as being anticipated by **Curtiss, III et al** (US Pat. 6,383,496) is traversed on the grounds that: "US Pat. No. 6,024,961) does not

teach or suggest an "attenuated" live bacteria with an altered Dam gene such that virulence of the attenuated bacteria reduced to an acceptable safety level."

8. In response to applicant's argument directed against US Pat. 6,383,496, that the reference fails to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., ***" live bacteria with an altered Dam gene** ) are not recited in the rejected claim(s) 3 and 4. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Claims 3 and 4 only require the attenuated live bacterium to evidence "(Dam) activity altered relative to the Dam activity of the wild-type" strain. This combination of claim limitations defines a **phenotype** of altered activity, that does not require the genotype to be a mutation in the Dam gene. Any gene or condition may be altered to result in the recited functional characteristic of an attenuated live bacterium with altered Dam activity.

Herithoff et al (1999) was cited to show that PhoP(-) strains have different amounts of Dam activity and Curtiss, III 6,383,496 claims priority back to US Pat. 6,024,961 which discloses at column 8, lines 52, 58 and 60 just such an avirulent, attenuated bacterial strain (see column 8, lines 45-64 of US Pat. 6,024,961, that would inherently evidence altered Dam activity. Arguments made of record in the Office Action dated August 21, 2003, paragraphs 6-7 (pages 3-6) are incorporated herein by reference.)

Additional Evidence was cited through providing Torreblanca et al (September 1996) who teach aro gene mutant strains of bacteria evidence altered Dam activity (see page 18, col. 2, Results section, first paragraph).

Curtiss, III et al at col. 55, Example 16, lines 65-66 ; col.56, lines 43-50; col. 58, lines 43-48 and col. 61, lines 19-46, especially lines 43-46, as well as (US Pat. 6,024,961 (priority document), col. 42, Example 10, lines 64-67; col. 42, lines 39-46; col. 45, lines 10-25) teach the importance of safe immunogenic compositions, which evidence enhanced and improved immunogenicity and safety, as live attenuated strains of bacteria with altered Dam activity. The reference inherently anticipates the instantly claimed invention of claims 3-4.

Atlas Powder Co. V IRECA, 51 USPQ2d 1943, (FED Cir. 1999) states "Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art...However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer. "The Court further held that "this same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art".

9. The rejection of claims s 1-4, 7-9 and 12 under 35 U.S.C. 102(b) as being anticipated by **Collier et al** (US Pat. 5,451,519) is traversed on the grounds that "[I]ndependent claim 1 is directed to a "immunogenic composition" wherein the "with the alteration [of the Dam activity] being in a manner which renders the live bacteria attenuated" does not disclose an immunogenic composition.

10. It is the position of the examiner that no evidence has been made of record showing that the compositions of Collier et al '519 are not immunogenic. While it is true that Collier et al teaches methods of cloning genes, the resulting compositions, comprise strains of E.coli bacteria that evidence altered Dam activity (Applicant agrees with this statement in the Response

Amendment , page 7, paragraph 3, top half of page). The carrier has not been so claimed to exclude the carrier/compositions of Collier et al, nor have the attenuated strains of Collier et al that evidence altered Dam activity been shown to structurally differ from that which is claimed.

The compositions of Collier et al comprise an attenuated strain of mutant E.coli that evidences altered Dam activity, broth and antibiotics (col. 20, lines 54-57), wherein E.coli is known to comprise immunogenic antigens (see Allan et al (US Pat. 5,747,309) who claims immunogenic attenuated strain containing compositions of E.coli) . The attenuated E.coli strains with altered Dam activity due to a mutation in the Dam gene were combined with an acceptable carrier "broth" together with antibiotics (this type of composition is safe, in view of the E.coli strain being attenuated relative to the wild type strain and broth and antibiotics serve as an acceptable pharmaceutical carrier (evidence provided by Applicant's specification, and US Pat.5,198,484 teaches that compositions that comprise broth and antibiotics together with a microorganism are safe (see US Pat. 5,198,484, claim 17) .

What is being claimed is not a Method, but compositions. A new use for an previously known composition, can be claimed as a method . The compositions of Collier et al inherently meet the structural and functional characteristics of the instantly claimed invention as E.coli is a known immunogen which was combined with an pharmaceutically acceptable carrier.

11. Applicant argues that the encoded T3 SAM modifying enzymes and the Bam HII methyl transferase are not "disclosed as an antigen that forms an immunogenic composition".

12. It is the position of the examiner that the expressed heterologous sequences need not be immunogenic portion of the claimed composition, but the entire composition must be

immunogenic; E.coli is a known immunogen (see US Pat. Allan et al, (US Pat. 5,747,309)). Applicant's arguments are not commensurate in scope with the instantly claimed invention.

13. The rejection of claims 1 and 7 under 35 U.S.C. 102(b) as being anticipated by **Anderson et al** is traversed on the grounds that Anderson does not teach or disclose bacteria which are attenuated by alteration of dam activity, and wherein "virulence of the attenuated bacteria is reduced to an acceptable safely level", nor an excipient that is pharmaceutically acceptable.

14. It is the position of the examiner that Anderson et al at column 5, lines 9-18, incorporates by reference the dam mutant type strains that are useful in the formulation of bacterial compositions that express heterologous antigens. Bale et al (1979) is cited and upon consideration of the focus of this reference, the phenotypic trains of 7 dam mutant strains of E.coli were evaluated, to include mutant strains that evidence decreased DNA adenine methylase activity in vivo and in vitro relative to the wild type parent strain. Anderson et al clearly teaches the utilization of dam mutant strains that evidence decreased dam activity, to include dam negative strains (see Bale et al abstract). The Dam negative mutant strains of E.coli utilized by Anderson et al are inherently attenuated, and express a heterologous antigen.

Additionally, the strains were combined with acceptable carriers (see col. 6, lines 15-20; col. 6, lines 52-67; col. 7, lines 1-5). The reference still inherently anticipates the instantly claimed invention. No evidence or structurally distinguishing characteristics for the claimed dam altered strains have been claimed so to remove Anderson et al as an applied reference.

15. Claims 1 and 7 rejected under 35 U.S.C. 102(a) as being anticipated by Shapiro et al (WO98/12206) is traversed on the grounds that: ccrM is not the same as Dam, and that Shapiro et al is directed to novel DNA methyltranferase genes.

16. It is the position of the examiner that what is claimed is a bacteria with altered DNA adenine methylase.

A methylase is an enzyme that catalyzes methylation of RNA or DNA (see Webster's Dictionary Definition attached herewith).

A methyltransferase is an enzyme that catalyzes the transfer of a methyl group from one compound to another (Dorlands Medical Dictionary)

Shapiro et al (WO98/12206) disclose an "essential adenine DNA methyltransferase (see page 12, paragraphs 3-4). The enzyme of Shapiro et al transfers a methyl group to adenine, thus defining a species of DNA adenine methylase based upon the broadest reasonable interpretation of the claims. No specific sequences are recited in the claims, only functional language is set forth to define the instantly claimed invention. The embodiment of Shapiro et al is not excluded from the claimed invention as the enzyme of Shapiro et al has the recited DNA adenine methylase activity, as it is an enzyme that methylates adenine DNA.

Despite the evidence submitted in the form of a published journal article to Kahng et al (2001), it is the position of the examiner that the claimed invention has not been structurally distinguished from the compositions disclosed in Shapiro et al. The mutant strain was combined with glycerol to form a bacterial glycerol stock (see page 37, paragraph e., bottom of page, first line. Glycerol is a known pharmaceutically acceptable carrier (US Pat. 5,952313, claim 5 and

USPat. 5,464,820, claim 7). The rejection is maintained for reasons of record in paper number 20, August 2003.

***Conclusion***

17. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (571) 272-0862. The examiner can normally be reached on 7:30-5:00 M-F, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Vgp
March 18, 2004

MARK NAVARRO
PRIMARY EXAMINER